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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GODDARD, LAURA B	
ART UNIT	PAPER NUMBER
1642	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/785,230	KISHIMOTO ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25, 26, and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 12, 2010 has been entered.

Claims 25, 26, and 28 are pending, amended, and currently being examined.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 25, 26, and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite “administering a substance” to treat a solid tumor, treat a disease pathologically caused by neovascularization, and to suppress vascularization, however, the claims never recite to what or where the substance is being administered. The metes and bounds of the claim cannot be determined. For the sake of compact prosecution, Examiner assumes the substance is being administered to a human.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 25, 26, and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state

of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method for treating a solid tumor comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human ligand SDF-1 and the human receptor CXCR4, wherein the substance is an anti-human CXCR4 antibody or a fragment thereof that binds to human CXCR4 (claim 25), a method for treating a disease pathologically caused by neovascularization comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human ligand SDF-1 and the human receptor CXCR4, wherein the substance is an anti-human CXCR4 antibody or a fragment thereof that binds to human CXCR4 (claim 26), a method for suppressing vascularization comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human ligand SDF-1 and the human receptor CXCR4, wherein the substance is an anti-human CXCR4 antibody or a fragment thereof that binds to human CXCR4 (claim 28).

The specification discloses that the structures of the receptor CXCR4 and its chemokine SDF-1 are known (p. 3-4; p. 14-16). The specification discloses that CXCR4 or SDF-1 knock-out mice show defective formation of the large vessel being supplied to the gastrointestinal tract (p. 4; p. 46-54). The specification contemplates using substances to inhibit CXCR4 or SDF-1 for use in the treatment of diseases involving

neovascularization (p. 5; p. 16-17). The specification contemplates antagonists such including an anti-SDF-1 antibody or anti-CXCR4 antibody (p. 17-18). The specification contemplates that vascularization inhibition will also have an antitumor effect as well as therapeutic effects on diseases pathologically caused by neovascularization (p. 38). The specification does not disclose any anti-human CXCR4 antibodies or fragments thereof that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization as claimed.

One cannot extrapolate the disclosure of the specification to the enablement of the claims because the specification does not provide any guidance or examples for making an anti-human CXCR4 antibody that inhibits the binding between the human ligand SDF-1 and the human receptor CXCR4 and predictably functions to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization. The specification fails to disclose a single representative species of antibody that functions as claimed. Examiner does not dispute that it is routine to screen for antibodies that bind known antigen CXCR4 and to screen for antibodies that inhibit binding between known ligand SDF-1 and CXCR4, however, it is undue experimentation to screen and produce an antibody that predictably functions to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization as claimed, and one of skill in the art could not reasonably extrapolate simple antibody binding to CXCR4 or SDF-1 ligand binding inhibition to that of treating a solid tumor, treating a disease pathologically caused by neovascularization, or

suppressing vascularization. Stancovski et al (PNAS, 1991, 88:8691-8695) demonstrate the unpredictable extrapolation of *in vitro* antibody function to *in vivo* effects. Stancovski et al showed that some antibodies binding HER2, a tumor expressed polypeptide, *in vitro* had a function of lysing tumor cells, however, when tested for effects *in vivo*, the effects of the antibodies were highly variable, wherein one antibody actually accelerated tumor growth. The differential tumor inhibitory potential of the antibodies did not correlate with cell lysis *in vitro* (Table 1; p. 8695, col. 1). Stancovski et al teach that they were unable to correlate the binding affinities of the antibodies or their affects on cell proliferation in cell culture with their actions on tumors (p. 8694, col. 2 to p. 8694, col. 1). Stancovski et al teach cell proliferation of HER2-expressing tumor cells in the presence of the monoclonal antibodies *in vitro* was a limited predictor of the anti-tumor potential of each antibody and it is possible there are processes only found *in vivo* that the antibodies interfere with (p. 8695, col. 1). Given the teaching of the Stancovski et al and the lack of disclosure in the instant specification of a single antibody that functions as claimed, one of skill in the art could not predictably or reasonably extrapolate the contemplation of producing anti-CXCR4 antibodies or CXCR4 antibodies that inhibit SDF-1 binding to that of treating a solid tumor, treating a disease pathologically caused by neovascularization, or suppressing vascularization. A high quantity of experimentation would be required to determine which antibodies would function as claimed.

Therefore, in view of the state of the art, the quantity of experimentation necessary, lack of guidance in the specification, and the absence of working examples,

it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Maintained Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 25, 26, and 28 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are drawn to a method for treating a solid tumor comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human ligand SDF-1 and the human receptor CXCR4, wherein the substance is an anti-human CXCR4 antibody or a fragment thereof that binds to human CXCR4 (claim 25), a method for treating a disease pathologically caused by neovascularization comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human

ligand SDF-1 and the human receptor CXCR4, wherein the substance is an anti-human CXCR4 antibody or a fragment thereof that binds to human CXCR4 (claim 26), a method for suppressing vascularization comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human ligand SDF-1 and the human receptor CXCR4, wherein the substance is an anti-human CXCR4 antibody or a fragment thereof that binds to human CXCR4 (claim 28).

The specification discloses that the structures of the receptor CXCR4 and its chemokine SDF-1 are known (p. 3-4; p. 14-16). The specification discloses that CXCR4 or SDF-1 knock-out mice show defective formation of the large vessel being supplied to the gastrointestinal tract (p. 4; p. 46-54). The specification contemplates using substances to inhibit CXCR4 or SDF-1 for use in the treatment of diseases involving neovascularization (p. 5; p. 16-17). The specification contemplates antagonists such including an anti-SDF-1 antibody or anti-CXCR4 antibody (p. 17-18). The specification contemplates that vascularization inhibition will also have an antitumor effect as well as therapeutic effects on diseases pathologically caused by neovascularization (p. 38). The specification does not disclose any anti-human CXCR4 antibodies or fragments thereof that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization as broadly encompassed in the claims.

The art (see Volin et al, Biochemical and Biophysical Research Communications, January 1998, 242:46-53, IDS; and Doranz et al, J Exp Med, October 1997, 186:1395-

1400, IDS) teaches monoclonal antibody 12G5 that binds CXCR4 (see Volin et al, p. 48; Figure 5; and see Doranz et al, p. 1397, col. 2, bottom; p. 1398, col. 1), however antibody 12G5 that binds CXCR4 does not provide an adequate representative number of species to support adequate written description for the broad genus of anti-human CXCR4 antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization as encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "treating a solid tumor," "treating a disease pathologically caused by neovascularization," or "suppressing vascularization," "anti-human CXCR4 antibody", "inhibits the binding between the human ligand SDF-1 and the human receptor CXCR4". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-

Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling

within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of anti-human CXCR4 antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization, per Lilly by structurally describing representative antibodies that function as claimed or by describing "structural features common to the members of the genus, which features

constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe anti-human CXCR4 antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses the structures of CXCR4 and SDF-1 are known, this does not provide a description of the broadly claimed anti-human CXCR4 antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization that would satisfy the standard set out in Enzo because the specification provides no structural features coupled to the claimed functional characteristics.

Further, the specification also fails to describe anti-human CXCR4 antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization by the test set out in Lilly because the specification describes only the structures of CXCR4 and SDF-1 and no antibodies that

function as claimed. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of anti-human CXCR4 antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization that is required to practice the claimed invention. Since the specification fails to adequately describe the product to which the claimed method uses, it also fails to adequately describe the method.

Response to Arguments

5. Applicants argue that the specification provides written description for anti-human CXCR4 antibodies that function (a) to inhibit the binding between the ligand human SDF-1 and the receptor human CXCR4 and (b) to treat a solid tumor, to treat a disease pathologically caused by neovascularization or suppress vascularization as claimed. Applicants argue that the production of antibodies to a known antigen is a rudimentary process achievable by a skilled artisan so long as the antigen is fully described. To that end, the specification discloses the amino acid and nucleotides sequences of human CXCR4 (SEQ ID NO: 1) (page 14, lines 24 to 26). Applicants argue that the specification further describes at least:

i. that both SDF- 1 and CXCR4 are necessary for neovascularization (page 2, line 20 to page 4, line 10);

ii. the structural of details of CXCR4 (page 2, line 20 to page 4, line 10);

iii. the role of SDF-1 (page 2, line 20 to page 4, line 10);

iv. anti-CXCR4 antibodies (page 18, lines 10 to 11);

v. how to make such anti-CXCR4 antibodies (page 26, line 25 to page 32, line 36); and

vi. methods of treating cancer, treating a pathology caused by neovascularization, and suppressing vascularization with such antibodies *(see* page 38, lines 15 to 25).

Applicants argue that the specification discloses the full sequence and the structure of the antigen, as well as antibodies that bind to the antigen and methods of making such antibodies. Applicants argue that each element of the claims is disclosed in the specification and one of skill in the art would recognize what is claimed in sufficient detail to reasonably conclude that the inventors were in possession of the claimed invention (see MPEP 2163).

The arguments have been considered but are not persuasive. Although the specification contemplates uses for the anti-CXCR4 antibody and methods of making them, the specification fails to disclose a single species of anti-CXCR4 antibody that functions to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization as claimed. Although both CXCR4 and SDF-1 are known antigens and *in vitro* screening for antibodies that bind CXCR4 and inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 can be routine, it is not routine to screen for antibodies that function to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress

vascularization *in vivo*. Further, the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to provide adequate written description for an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

6. Applicants point to Forster (J. Immunol. 160:1522-1531, 1998), and argue that it discloses evidence of antibodies that bind to CXCR4 and thereby inhibit a downstream HIV- 1 infection. As evidenced by Crump (EMBO J. 16: 6996-7007, 1997, attached hereto), CXCR4 functions as a corecpetor for HIV- 1, and HIV- 1 inhibits SDF- 1 from binding to CXCR4. Thus it is apparent that the HIV- 1 binding site on CXCR4 shares the SDF- 1 binding site. Therefore, inhibiting HIV- 1 binding with an antibody will also inhibit the binding of SDF- 1. The methods of Forster recite routine production of antibodies using techniques well known in the art at the time of the present application. Applicants argue that Forster demonstrates production of antibodies that inhibit the binding of SDF-1 to CXCR4 through the starting point of simply knowing the antigen. Applicants argue that the specification in combination with Forster, therefore, demonstrates to one of ordinary skill in the art that Applicants were in possession of the claimed invention.

The arguments have been considered but are not persuasive. Forster et al teach an antibody that binds to CXCR4, and using the antibody to detect CXCR4 expression on lymphoid cells and to neutralize infection of cells with HIV-1. Crump et al teach determining the three-dimensional structure of SDF-1 and that SDF-1 analogs could block HIV-1 entry via CXCR4, which is and HIV-1 coreceptor. Neither of these

references demonstrate making an antibody that functions to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization. While methods of making an antibody that binds a known antigen or that inhibits binding between known ligand and receptor may be routine, making and using and antibody that functions to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization is not and the specification fails to disclose a single representative antibody that functions as claimed.

7. Applicants argue that their previous response pointed to support from similar cases supporting the notion that full disclosure of the antigen provides adequate written description for an antibody against the antigen. *Noelle v. Lederman,* 355 F.3d 1343, 1349 (Fed. Cir. 2003) states that "as long as an applicant has a *'fully characterized* antigen' by its structure, formula, chemical name, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen." Applicants argue that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. *In re Wertheim,* 541 F.2d 257, 262, (CCPA 1976). Accordingly, as the specification has fully characterized the antigen, as well as the interaction between the ligand and receptor, an antibody claimed by its binding affinity is described.

The arguments have been considered but are not persuasive. Examiner agrees that Applicants are in possession of the genus of antibodies that bind fully characterized antigen CXCR4 and even the genus of antibodies that can inhibit the binding between

the known human ligand SDF-1 and the human receptor CXCR4, however, the specification fails to disclose a single species of antibody that functions to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization.

8. Applicants argue that the Examiner appears to refute this rule of law with the nuanced assertion that antibodies that inhibit the binding of SDF- 1 and treat a tumor, a disease pathologically caused by neovascularization, or suppressing vascularization are not described. The Examiner alleges that such treatments are not routine. Applicants argue that all of the claims are directed to inhibiting SDF-1 from binding to CXCR4 by blocking the binding site for SDF-1 with an antibody. As discussed above, and as demonstrated by Forster, such antibodies are produced routinely once the full antigen is known. The Examiner has raised no objection to the fact that the antigen is fully described. The downstream vascularization consequences of SDF- 1 binding to CXCR4 are described, and as such, inhibiting the vascularization signaling cascades turned on by the interaction between SDF- 1 and CXCR4 by preventing SDF- 1 binding are consequences of the antibody binding. Further, with regard to *In re Alonso,* the Examiner refutes Applicants' previous arguments that this decision is inapplicable, as Applicants have not produced one species of antibody. Applicants argue that production of an antibody is not required for evidence of adequate written description. As found in *Noelle,* description of a full antigen is sufficient for describing antibodies directed against it. Applicants argue that MPEP 2163.07(a) states that by disclosing in a patent

application a device (i. e. antibody) that inherently performs a function or has a property, operates according to a theory or has an advantage (i. e. blocking the interaction between SDF-1 and CXCR4), a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. Accordingly, by disclosing the interaction between SDF- 1 and CXCR4 and antibodies to those proteins, the inherent function of blocking the interaction with an antibody is described.

The arguments have been considered but are not persuasive. Examiner agrees that Applicants are in possession of the genus of antibodies that bind fully characterized antigen CXCR4 and even the genus of antibodies that can inhibit the binding between the known human ligand SDF-1 and the human receptor CXCR4, however, the specification fails to disclose a single species of antibody that also functions to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization. The specification does not disclose or exemplify a single agent that when administered, binds CXCR4, inhibits binding between SDF- 1 and CXCR4, and treats a solid tumor, treats a disease pathologically caused by neovascularization, or suppresses vascularization.

9. Applicants argue that *Lilly* and *Enzo* concerned issues regarding the DNA sequences not being disclosed. *Noelle,* a later issued decision by the Federal Circuit, clearly states that antibodies derived from a fully disclosed antigen are satisfied for purposes of written description, thereby nullifying any applicability *of Lilly* and *Enzo,*

which do not concern antibodies. Similarly, the Examiner's reliance *of Rochester v. Searle,* 358 F.3d 916 (Fed. Cir. 2004), is not applicable to the claimed invention. *Rochester* concerned claiming small chemical compounds to inhibit the activity of a prostaglandin H synthase-2 (PGHS-2) when such compounds had not been identified. However, antibodies are well known compounds in the art, and can be readily produced. It appears as though the Examiner is applying *Rochester* for the notion that a variable domain on an antibody had not been identified. This is very different from a completely theoretical compound that could comprise any number of molecules and could be of any size. Antibodies, unlike the issues in *Rochester,* are well described, characterized and understood in the art. Unlike *Rochester,* one skilled in the art can immediately recognize how to make and produce the claimed invention based on the specification.

The arguments have been considered but are not found persuasive. The concepts of decisions in *Lilly* and *Enzo* are relevant. A stated previously: The specification does not disclose even one representative species of antibody that functions as claimed. The specification and claims do not define the structural features commonly possessed by members of the antibody genus that can distinguish it from others. There is no recitation or disclosure of structural features common to the members of the antibody genus or which features constitute a substantial portion of the genus. The specification and claims do not identify which structural features are conserved among the claimed antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a

disease pathologically caused by neovascularization, or suppress vascularization or which structures constitute a substantial portion of the genus in order for one to visualize or recognize the identity of the members of the genus, hence the written description for the genus of antibodies in the claimed methods do not meet the standards of Lilly. There are no specific structures, identifying characteristics, partial or complete structures, or known or disclosed structures coupled to the functional characteristic for the broad genus of antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization as recited in the claims, hence the specification does not provide adequate written description according to the standards of Enzo. Applicants were not in possession of the genus of antibodies at the time of filing.

The concept of the decision found in *Rochester v. Searl* is relevant to the instant claims. The court found that screening assays are not sufficient to provide adequate written description for an invention because they are merely a wish or plan for obtaining the claimed chemical invention. Although general antibody structures are known, the required antibody structure, required variable domains, or required amino acid sequences to make an antibody that functions to treat a solid tumor, treat a disease pathologically caused by neovascularization, or suppress vascularization are never disclosed. Screening for antibodies that function to inhibit the binding between the human ligand SDF-1 and the human receptor CXCR4 and treat a solid tumor, treat a

disease pathologically caused by neovascularization, or suppress vascularization, is not routine and is a wish or plan for obtaining the claimed invention.

10. **Conclusion:** No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on 571-272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Laura B Goddard/
Primary Examiner, Art Unit 1642